

REMARKS

In the final office action mailed March 30, 2005, the Examiner objected to the specification for not including the relationship between the priority applications. Claims 25-27 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement, under 35 U.S.C. § 102(b) and (e), as being anticipated, and under 35 U.S.C. § 103(a), as obvious. Claims 25-27 were rejected under the doctrine of obviousness-type double patenting over claims 1-4 of U.S. Patent No. 6,187,287 and over claims 1, 9, 20-21, 25-26 and 29-30 of U.S. Patent No. 5,789,554. The specific grounds for objection, and Applicants' response thereto are set out in detail below.

Claims 28-32 have been added and claims 25-27 have been canceled. Support for steps (a), (b), (c), (d) and (e) of claim 28 can be found in the specification at paragraph [0043]. Additional support for step d of claim 28 can be found in the specification at paragraph [0067], last sentence. Support for claim 29 can be found in the specification at paragraphs [0043] and [0067]. Support for claim 30 can be found in the specification at paragraphs [0043] and [0067]. Support for claim 31 can be found in the specification at paragraph [0043], last sentence. Support for step (f) of claim 32 can be found in the specification at paragraph [0044], first sentence and Examples 2 and 3. Support for step (g) of claim 32 can be found in the specification at paragraphs [0044, 0045 and 0046]. Support for step (h) of claim 32 can be found in the specification at paragraph [0053]. Support for step (i) of claim 32 can be found in the specification at paragraph [0048].

Claims 28-32 are pending for consideration, which is respectfully requested in view of the foregoing claim cancellations and additions, and the following remarks.

I. Formalities

A. Specification

The Examiner has objected to the specification for not including the relationship between the priority applications. The Examiner also asserts that the instant application is a continuation-in-part of United States Application No. 09/741,843 (rather than a continuation) because the instant application discloses the limitation of a variable light chain CDR3 consisting of amino acids 95-102, which alleged is not supported in United States Application No. 09/741,843.

In response applicants have requested herein amendment of the specification to include the relationship between the priority applications. Applicants submit that this amendment satisfies the examiner's objection. As such, withdrawal of the objection respectfully is requested.

II. Rejection under § 112, first paragraph

Claims 25-27 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable the scope of the humanized LL2 antibodies and fragments claimed. Applicants respectfully traverse.

Applicants submit that one skilled in the art would readily be able to readily determine and generate the full scope of antibodies and fragments encompassed by the scope of claims 25-27 by employing no more than routine experimentation. Nevertheless, without acquiescing in any way in the propriety of the rejection, Applicants have canceled claims 25-27 thereby mooting the rejection as to those claims.

In addition, applicants submit that the examiner's concern regarding whether or not one skilled in the art could predictably substitute at least one amino acid in the framework regions of the heavy and light chain variable regions of the LL2 monoclonal antibody with reasonable expectation of success of maintaining antibody function is irrelevant to newly added claims 28-32. Accordingly, withdrawal of the rejection respectfully is requested.

III. Rejections under 35 USC § 102

Claims 25-27 are rejected under 35 U.S.C. § 102(b) as anticipated by Pawlak-Byczkowska *et al.*, Goldenberg *et al.*, Kreitman *et al.*, Juweid *et al.*, Goldenberg (US Patent 5,776,094), Murthy *et al.*, and two publications by Leung. Claims 25-27 have been canceled, thereby rendering moot the rejection as to those claims.

In addition, Applicants submit that added claims 28-32 are not anticipated by any of the references cited by the Examiner. Specifically, the added claims are directed to the design and preparation of humanized antibody variable domains by combining antibody framework (FR) regions with the complementarity determining regions (CDRs) from a monoclonal antibody that is to be humanized, where at least two of the antibody FRs are from different human monoclonal antibodies. None of the cited describe the methods of claims 28-32. More specifically, none of

references, either alone or in combination, suggest that humanized variable domains can be prepared that incorporate at least two antibody framework regions from different human monoclonal antibodies.

Applicants note that in order to reject a claim under 35 USC § 102, the Examiner must demonstrate that each and every claim limitation is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (August 2001). None of the cited references describe each and every element of the instantly claimed invention and therefore applicants respectfully request that the rejection under 35 USC § 102 be withdrawn.

IV. Rejections under 35 USC § 103

The Examiner alleges that claims 25-27 are obvious under 35 U.S.C. § 103(a) over Pawlak-Byczkowska *et al.* as evidenced by Kreitman *et al.*, in view of Queen (U.S. Patent 5,530,101), Goldenberg *et al.* and Orlandi *et al.* Claims 25-27 have been canceled, thereby rendering the rejection moot as it applies to those claims. To the extent that the Examiner seeks to apply the rejection to added claims 28-32, Applicants respectfully traverse.

All claims are presumed initially to be non-obvious. A *prima facie* case of obviousness requires three elements: (1) a teaching or suggestion of all of the claim limitations; (2) a suggestion or motivation to modify or combine the teachings of the applied prior art; and (3) a reasonable expectation of success in reaching the claimed invention. The Examiner bears the initial burden of supporting any *prima facie* assertion of obviousness with adequate facts. MPEP § 2142 (Feb. 2000).

Here, none of the cited references, either alone or in combination, disclose all the elements of claim 28. Accordingly, the first element of a *prima facie* case of obviousness cannot be satisfied and withdrawal of the rejection respectfully is requested.

V. Rejections for Obviousness-Type Double Patenting

Claims 25-27 are rejected under the doctrine of obviousness-type double patenting over claims 1-4 of U.S. Patent No. 6,187,287 and over claims 1, 9, 20-21, 25-26 and 29-30 of U.S. Patent No. 5,789,554. This rejection is rendered moot by the cancellation of claims 25-27.

CONCLUSION



In view of the above remarks and amendments, Applicants respectfully submit that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, Applicants authorize the Commissioner to charge any deficiency to Deposit Account No. 08-1641.

Respectfully submitted,

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